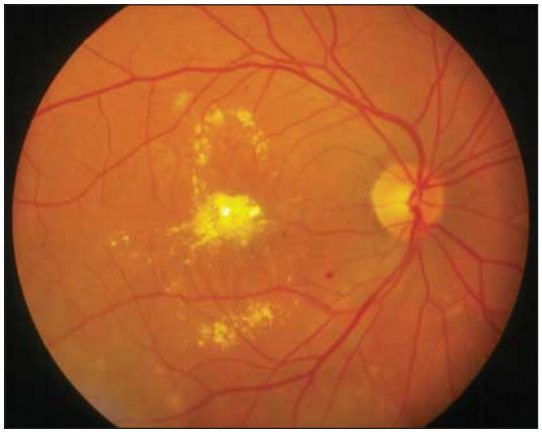
# Clinical review

*Extracts from "Concise Clinical Evidence"*

## Diabetic retinopathy

Simon Harding

**Definition** Diabetic retinopathy is characterised by varying degrees of microaneurysms, haemorrhages, exudates (known as hard exudates in the United States), venous changes, new vessel formation, and retinal thickening. It can involve the peripheral retina or the macula, or both. The range of severity of retinopathy includes background (mild non-proliferative), preproliferative (moderate or severe non-proliferative), proliferative, and advanced retinopathy. Involvement of the macula can be focal, diffuse, ischaemic, or mixed.



SUE FORD/SPL

Eye with diabetic maculopathy

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### What are the effects of treatments for diabetic retinopathy?

### Beneficial

**Macular photocoagulation**
In people with clinically significant macular oedema, one large randomised controlled trial (RCT) has found that laser photocoagulation to the macula versus no treatment significantly reduces visual loss at three years in eyes with macular oedema and mild to moderate diabetic retinopathy, with some evidence of greater benefit in eyes with better vision. Subgroup analysis found that focal laser treatment was significantly more effective in reducing visual loss in eyes with clinically significant macular oedema, particularly in people in whom the centre of the macula was involved or imminently threatened.

**Peripheral retinal laser photocoagulation**
In people with preproliferative (moderate or severe non-proliferative) retinopathy and maculopathy, RCTs involving eyes with preproliferative retinopathy and maculopathy have found that peripheral retinal photocoagulation versus no treatment significantly reduces the risk of severe visual loss at five years.

**Peripheral retinal laser photocoagulation**
In people with proliferative retinopathy, RCTs have found that peripheral retinal photocoagulation versus no treatment significantly reduces the risk of severe visual loss at 2-3 years. One RCT involving eyes with high risk proliferative diabetic retinopathy found that low intensity versus standard intensity argon laser significantly reduced vitreous haemorrhage and macular oedema. It found no significant difference between treatments for visual acuity, although it may have lacked power to detect clinically important effects.
(For evidence of benefits of control of diabetes, see glycaemic control in diabetes; of control of hypertension, see primary prevention; of smoking cessation, see primary prevention, all on www.clinicalevidence.com)

### Likely to be beneficial

**Grid photocoagulation to zones of retinal thickening**
In people with diabetic maculopathy, one RCT found a significant improvement in visual acuity in eyes treated with grid photocoagulation versus untreated eyes at 12 months and at 24 months. Photocoagulation versus no photocoagulation reduced the risk of moderate visual loss by 50-70%.

### Unknown effectiveness

**Macular photocoagulation**
We found no RCTs of macular photocoagulation in people with maculopathy but without clinically significant macular oedema.


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**Peripheral retinal laser photocoagulation**
We found no RCTs in people with background or pre-proliferative (non-proliferative) retinopathy without maculopathy.

## What are the effects of treatments for vitreous haemorrhage?

### Likely to be beneficial

**Vitrectomy**
In eyes with severe vitreous haemorrhage and proliferative retinopathy, one RCT found that early versus deferred (for one year) vitrectomy significantly reduced visual loss at one, two, and three years. Subgroup analysis showed significant benefit in people with type 1 diabetes but not those with type 2 diabetes.

### Unknown effectiveness

**Vitrectomy in people with maculopathy**
The role of vitrectomy in people with maculopathy remains unclear.

The full content of Clinical Evidence is available online (www.clinicalevidence.com); topics are updated every eight months.

# Commentary: Treatment of diabetic retinopathy

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Diabetic retinopathy remains the commonest cause of visual loss in the working age population, even though laser treatment has been available now for nearly 30 years. Can anything else can be done besides treating the sight threatening lesions with photocoagulation?

Strict control of diabetes will reduce both the incidence and the progression of early retinopathy. This has been shown for type 1 diabetic patients in the diabetes control and complications study and for type 2 patients by the United Kingdom prospective diabetes study.[1 2] In the former study, the strict control group maintained 1% lower glycated haemoglobin and this resulted in a 25% reduction in microvascular end points, most marked in the need for photocoagulation. For every 1% reduction in glycated haemoglobin there is a 37% decrease in laser treatment and a 10% reduction in cataract extraction.[3]

In the United Kingdom prospective diabetes study, over half of the patients had high blood pressure or were being treated for it. Tight control of the blood pressure, aiming at below 150/90, had a significant beneficial effect reducing the incidence of retinopathy and its progression to photocoagulation.[4] For every 10 mm reduction in the systolic blood pressure there was an 11% reduction in the need for laser treatment. The effect was similar whether β blocker or angiotensin converting enzyme inhibitor was used. Only 10% of patients with tight control of blood pressure lost three lines of visual loss on the Snellen chart, while in the less tightly controlled group 20% did so (unpublished data).

Unexpectedly, smoking had no deleterious effect on retinopathy in the United Kingdom prospective diabetes study. Indeed, fewer current smokers needed laser therapy and cataract extraction than among those who never smoked or had stopped smoking.

Laser treatment is effective in treating sight threatening retinopathy, proliferative retinopathy, and maculopathy characterised by fluid accumulation in the immediate vicinity of the fovea (clinically significant macular oedema). The greatest effect is in proliferative retinopathy, where with adequate and timely treatment useful central vision can be maintained in up to 90% of patients. This is often achieved only by sacrificing peripheral vision, which in many patients excludes driving and in some causes difficulty in night vision. Adequate laser treatment often prevents vitreous haemorrhage, and even if it occurs the outcome is often better after vitrectomy if laser treatment has been performed.

In proliferative retinopathy, especially in younger patients, treatment has to be carried out as soon as possible after diagnosis. These vessels often progress and bleed within days or weeks.

Vitrectomy is usually successful in certain forms of advanced diabetic retinopathy: non-clearing vitreous haemorrrhage, traction on the macula, and retinal detachment involving the macula. These complications occur in some cases of proliferative retinopathy, if not treated in good time or adequately.

Maculopathy leads to less dramatic visual loss and its progression is much slower. Laser treatment depends on the type of lesions present; in the commonest form, exudative maculopathy, treating the centre of hard exudate rings is most effective. Laser treatment is less effective in maculopathy than proliferative retinopathy, mainly because many patients have ischaemia at the fovea, which is not responsive to treatment. Most patients already have visual loss when presenting for treatment. The aim is to slow down the process and maintain vision rather than improve it. A 10 year follow up of laser treatment for maculopathy found that patients with exudative lesions and good vision at entry were likely to maintain this, while those with ischaemic and diffuse lesions fared much worse.[5]

Coexistence of proliferative retinopathy and macular oedema is not uncommon. Formal clinical trials have not been carried out in this condition, but it is "usual" to treat the proliferative lesions first in young

patients, often with spontaneous resolution of the macular oedema. In type 2 patients, especially if they are older, it is best to treat the macula first, as extensive peripheral laser treatment may worsen macular oedema.

None of the treatments currently available is totally effective, but several clinical trials now in progress may find newer more effective treatments to prevent visual loss.

Competing interests: EK had a grant from MRC and NEI, and has acted as an expert witness.

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4 United Kingdom Prospective Study Group. Tight blood pressure control and risk of macro and microvascular complications in type 2 diabetes (UKPDS 38). *BMJ* 1998;317:703-13.
5 Davies EG, Petty RG, Kohner EM. Long term effectiveness of photocoagulation for diabetic maculopathy. *Eye* 1989;3:764-7.

*Lesson of the week*

# Zosteriform metastasis from melanoma

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**Cutaneous metastases from primary tumours, including malignant melanoma, can imitate herpes zoster (shingles)**

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Approximately 10% of metastases from all primary neoplasms involve the skin, but for malignant melanoma the figure is 44%.[1] In some cases of melanoma this is the presenting feature, either because the primary lesion has regressed completely or because it has been unnoticed or ignored by the patient. Occasionally the melanoma has originated at an extracutaneous site such as the retina or the anal canal.

Metastases from cutaneous melanoma normally present as flesh coloured papules or nodules in the skin. Only about a third are pigmented or ulcerated. We report a case in which cutaneous metastases from a melanoma imitated herpes zoster. This presentation is known as zosteriform metastasis; it also occurs with other neoplasms.

## Case report

A 73 year old white man presented with a three week history of painful, pruritic vesicles on a background of erythema on the right frontal area of the scalp (figure). The lesion had not responded to self prescribed topical antibiotics and antiseptics. The patient had grown up in South Africa and had a history of excessive exposure to the sun. He had previously developed three basal cell carcinomas and had numerous actinic keratoses. Five years earlier a malignant melanoma, Breslow thickness 1.25 mm, had been excised from his right shoulder. At that time there had been no evidence of metastatis. He had been followed up regularly and there had been no evidence of recurrence. He also had a five year history of stage Ib mycosis fungoides.

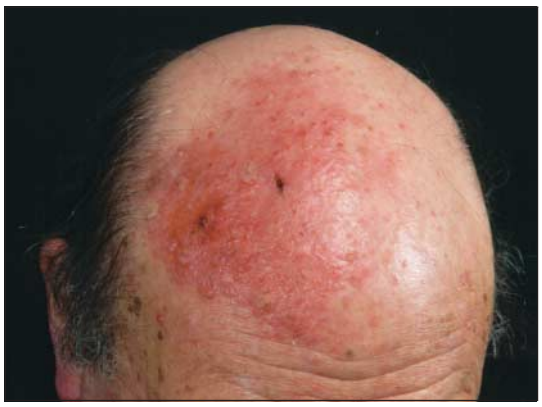
Clinical examination showed that the lesion lay within the area supplied by the ophthalmic branch of the right trigeminal nerve. A provisional diagnosis of herpes zoster (shingles) was made, and he was treated with 800 mg of oral aciclovir five times a day. There was no history of herpes zoster at the same site or elsewhere.

He was reviewed seven days after starting aciclovir. The lesions had extended slightly but otherwise remained unchanged. At that point a diagnosis of plaque stage mycosis fungoides was considered, and the scalp lesion was biopsied. Histological examination showed that the dermis was heavily infiltrated by non-pigmented malignant cells, which were epithelioid in appearance and forming nests; immunostaining showed that these cells were metastatic melanoma.

The area was too extensive to excise. After discussion with the patient the lesion was treated with electron beam radiotherapy (40 Gy in 15 fractions). The response was dramatic and within a few weeks the lesion regressed almost completely except for some residual macular erythema.

## Discussion

Many different malignant tumours can metastasise to the skin but the commonest primary sources are tumours of breast, stomach, lung, and uterus. These lesions usually present as firm papules or nodules, both of which may ulcerate; occasionally they are inflammatory, sclerotic, bullous, or vesicular. Zosteriform metastasis is less well known; it may arise from adenocarcinoma of the lung,[2 3] carcinoma of the prostate,[4 5] Kaposi's sarcoma,[6 7] transitional cell carcinoma of the bladder,[8] or malignant melanoma.[9 10] Zosteriform metastases are usually painful, tender, or pruritic and consist of vesicles on a background of erythema,



Zosteriform metastasis from malignant melanoma